

Figure 1A

SEQ I D NO:

49 49 50 50 50	99 99 100	149 149 149 150	199 199 198 198 200
QHL AHCVPKI QHL AHYVPKI HHL AQL VPEI HHL AQL VPEI	E QANK P S HL C E QANK P S HL C KHS G- AF QL C KHS G- AF QL C	MTTSGGGGFC MTTSGGGGFC MHTSTGGGFC MHTSTGGGFC M TS. GGGFC	RTYNI FAI MF RTYNI FAI TF QARRI FPSVI QARKI FPSVI
QAT DL NREVY QAT DL TREVY QQV DF YT AF L QQV DF YT AF L Q D	EDPALGFPKL EDPAFGFPKL EDPDICLEKL EDPDICLEKL EDPDICLEKL	GSI HRDHRYR GSI HRDHRYR SSVHKNHRYK DSVHKNHRYK	GPYCQKHKLS SSEVVEEEDP LVHLSEDVI A RTYNI FAI MFGPYCQKHELN TSEI EEEEDP LVHLSEDVI A RTYNI FAI TFGPYCQKHELN TSEI EEEEDP LVHLSEDVI A QARRI FPSVI GPFCVNHEPG RAGTI KENSR - CPLNEEVI V QARKI FPSVI GP. CHEIF
S AEE! AGRWL S AEE! AGKWL AP QRP AS WWD TP QRL AS WWD	LGPMEWYICA LGPMEWYLCG LTPLEWYLFG FTPLEWYLFG L.P.EWYLG	TCVLCMECFL TCVLCMECFL TCVLCMDCFQ TCVLCMDCFQ TCVLCMCFQ	GPYCQKHKLS SSEVVEEEDP GPYCQKHELN TSEIEEEEDP SPFCVDHEPG RAGTTKESLH GPFCVNHEPG RAGTIKENSR GP. C HE
AI D- RSLLEC AI D- RSLLEC RMDVSPEPPL RMEI SAELPQ DL	KEDTLAQHIL KEDMLAQHVL KQEESVQMSI KQEESVQMSI KQEESVQMSI	YSCRDCAVDP YSCRDCAVDP YSCRDCAI DP YSCRDCAI DP YSCRDCAI DP	GPYCOKHKLS SSEVVEEEDP GPYCOKHELN TSELEEEEDP GPFCVDHEPG RAGTTKESLH GPFCVNHEPG RAGTIKENSR GP.CHEE
MASENEPEVQ MASELEPEVQ MADEEMDGAE MADEEAGGTE	YCRGPNPFPQ YCRGPNPFPQ YFAEMDPDLE YFAEMDPDLE YFAEMDPDLE	GRVFKVGEPT GRVFKVGEPT GKVFKSGETT GRVFKSGETT GRVFKSGETT	DCGDTE AWKE DCGDTE AWKE DCGDTE AWKT DCGDTE AWKT DCGDTE AWKT
mous e_E3al I huma n_E3al I mous e_E3al huma n_E3al Cons ens us	mous e_E3al I human_E3al I mous e_E3al human_E3al Cons ens us	mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3αI Cons ens us	mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3αI Cons ens us
6 · 4 15 2	6 1 5 2 2	6 1 1 5 2 2	6 4 1 2

Figure 1B

249 249 248 248 250	298 298 298 298 300	348 348 348 350
EQVI YTLQKA EQVI YTLQKA DHVI YSLQRA DHVI YSLQRA	NT S R QTK-PL NT S R QTK-PL HS E NV S QHPL HS E NV S QHPL	KVQVMHSSVA AHQNFGLKAL SWLGSVIGYS DGLRRILCQV GLQEGPDGEN KVQVMHSSIV AHQNFGLKLL SWLGSIIGYS DGLRRILCQV GLQEGPDGEN 4VEVLHSVVM AHQKFALRLG SWMNKI MSYS SDFRQIFCQA CLVEEPGSEN HVEVLHSEIM AHQKFALRLG SWMNKI MSYS SDFRQIFCQA CLREEPDSEN VV. V. HS AHQ. F. L. L. SWI. YS R. I. CQ L. E. PD. EN
KESELPEDLE VAEKSDTYYC MLFNDEVHTY EQVIYTLQKA KESELPADLE MVEKSDTYYC MLFNDEVHTY EQVIYTLQKA EEKELPPELQ IREKNERYYC VLFNDEHHSY DHVIYSLQRA EEKELPPELQ IREKNERYYC VLFNDEHHSY DHVIYSLQRA . E. ELP L EK YYC . LFNDE. H. Y VIY. LQ. A	VNCTQKEAI G FATTVDRDGR RPVRYGDFQY CDQAKTVI VR NTSRQTK- PL VNCTQKEAI G FATTVDRDGR RSVRYGDFQY CEQAKSVI VR NTSRQTK- PL -DCELAEAQL HTTAI DKEGR RAVKAGVYAT CQEAKEDI KS HSENVSQHPL LDCELAEAQL HTTAI DKEGR RAVKAGAYAA CQEAKEDI KS HSENVSQHPL CEATDGR R.VG CAKI	KVQVMHSSVA AHQNFGLKAL SWLGSVIGYS DGLRRILCQV GLQEGPDGEN KVQVMHSSIV AHQNFGLKLL SWLGSIIGYS DGLRRILCQV GLQEGPDGEN 4VEVLHSVVM AHQKFALRLG SWMNKIMSYS SDFRQIFCQA CLVEEPGSEN HVEVLHSEIM AHQKFALRLG SWMNKIMSYS SDFRQIFCQA CLREEPDSEN VV. V. HS AHQ. F. L. L. SW YS R. I. CQ L. E. PD. EN
VAEKSDTYYC MVEKSDTYYC I REKNERYYC I REKNERYYC EK YYC	RPVRYGDFQY RSVRYGDFQY RAVKAGVYAT RAVKAGAYAA R. V G	SWLGSVIGYS SWLGSIIGYS SWMNKIMSYS SWMNKIMSYS
KESELPEDLE KESELPADLE EEKELPPELQ EEKELPPELQ EEKELPPELQ	'NCTQKEAI G FATTVDRDGR RPVRYGDFQY 'NCTQKEAI G FATTVDRDGR RSVRYGDFQY DCELAEAQL HTTAI DKEGR RAVKAGVYAT 'DCELAEAQL HTTAI DKEGR RAVKAGAYAA 'CEAT.D.GR R.V.G	AHONF GL KAL AHONF GL KL L AHOKF AL RL G AHOKF AL RL G
RYAVDI LTWE I RYAVEI LTWE I KYI VEMTI WE E KYVVEMTI WE I Y. VE WE	VNCTOKEAI G VNCTOKEAI G L DCEL AEAQL L DCEL AEAQL	KVQVMHSSVA KVQVMHSSI V HVEVLHSVVM HVEVLHSEI M . V. V. HS
mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3αI Cons ens us	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us
6 1 1 5 2	6 4 4 2 2 2	6 4 4 2 2

Figure 1C

Figure 1D

498 498 496 496	548 548 546 546	598 598 595 595
LDLKYVLI SK PTEWS DELRO LDLKYVLI SK PTEWS DELRO CDLKYI LI SK PVI WTERLRA CDLKYI LI SK PTI WTERLRM DLKY. LI SK PT. W LR.		
_	EWEPEWEAAF TLOMKLTHVI EWEPEWEAAF TLOMKLTHVI EVDPDWEAAI AIOMOLKNIL EVDPDWEAAI AIOMOLKNIL E. P. WEAAOM L	SMVQDWCALD EKVLIEAYKK CLAVLTQCHG GFTDGEQPIT LSICGHSVET SMWQDWCASD EKVLIEAYKK CLAVLMQCHG GYTDGEQPIT LSICGHSVET LMFQEWCACD EDLLLVAYKE CHKAVMRCST NFMSSTKTV- VQLCGHSLET LMFQEWCACD EELLLVAYKE CHKAVMRCST SFISSSKTV- VQSCGHSLET M.O. WCA. D. F. I. AVK. C. M. C. M. C. WCA. D. F. I. AVK. C. M. C. WCA. D. F. M. C. WCA. D. F. I. AVK. C. WCA. D. F. I. AVK. C. M. C. WCA. D. F. I. AVK. C. M. C. WCA. D. F. I. AVK. C. WCA. D. F. I. AVK. C. M. C. WCA. D. F. I. AVK. C. WCA. D. F. M. C. WCA. D. F. I. AVK. C. WCA. D. F. I. AVK. C. WCA. D. F. I. A
FKFRRVQSLI FKFRRVQSLI DKLGRVYAVI DKLGRVYAVI	PI TRQVGQHI PI TRQVGQHI EI RRQVGQHI EI RRQVGQHI	CLAVLTQCHG CLAVLMQCHG CHKAVMRCST CHKAVMRCST
KHRDAQGRF QFERYTALQA FKFRRVQSLI RHRDAQGRF QFERYTALQA FKFRRVQSLI PEYLDRNN- KFN-FQGYSQ DKLGRVYAVI PEYLDRNN- KFN-FQGYSQ DKLGRVYAVI	(FLGGFDAFL ELLKCMQGMD PITRQVGQHI KFLEGFDAFL ELLKCMQGMD PITRQVGQHI VFLEGFRSFL KILTCMQGME EIRRQVGQHI OFLEGFRSFL KILTCMQGME EIRRQVGQHI FLEGF. FLL.CMQGM. I.RQVGQHI	MYQDWCALD EKVLIEAYKK CLAVLTQCHG GFTDGEQPITION OF THE GYTDGEQPITION OF THE GYTDGE GYTDGE GYTDGEGOPITION OF THE GYTGGEGOPITION OF THE GYTGGEG
L KHRDAQGRF L RHRDAQGRF L PEYL DRNN- L PEYL DRNN-	KFLOGFDAFL ELLKCMQGMD KFLEGFDAFL ELLKCMQGMD QFLEGFRSFL KILTCMQGME QFLEGFRSFL KILTCMQGME OFLEGF.FL KILTCMQGME	S MV QDWCAL D S MWQDWCAS D L MF QE WCACD L MF QE WCACD M O. WCA. D
SEQ I D NO: 6 mouse_E3aII 4 human_E3aII 15 mouse_E3aI 2 human_E3aI Consensus	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E 3aI Cons ens us	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us
SEQ 6 4 15 2	6 1 1 5 2 2	6 1 1 5 2

Figure 1E

648 648 645 645	698 698 695 700	748 748 738 738
_		
RYCVSQEKV SIHLPISRLL AGLHVLLSKS EVAYKFPELL PLSELSPPMLYCVSQEKV SIHLPVSRLL AGLHVLLSKS EVAYKFPELL PLSELSPPMLSYKVSEDLV SIHLPLSRTL AGLHVRLSRL GAISRLHEFV PFDSFQVEVLXSYRVSEDLV SIHLPLSRTL AGLHVRLSRL GAVSRLHEFV SFEDFQVEVLXY.VSV SIHLP.SR.L AGLHV.LSE.	CAQVHAGMMR RNGFSLVNQI YYYHNVKCRR EMFDKDI VML CAQVHAGMMR RNGFSLVNQI YYYHNVKCRR EMFDKDVVML VAQVVAEMMR RNGLSLI SQV FYYQDVKCRE EMYDKDI I ML VAQVVAEMMR RNGLSLI SQV FYYQDVKCRE EMYDKDI I ML · AQV. A. MMR RNG. SL. Q. · YY. · VKCR. EM. DKDI . ML	OTGVSMMDPN HFLM MLSRF ELYQLFSTPD YGKRFSSEVT HKDVVQQNNT OTGVSMMDPN HFLM MLSRF ELYQIFSTPD YGKRFSSEIT HKDVVQQNNT OIGASI MDPN KFLLLVLQRY ELTDA FNKTISTK DQDLI KQYNT OIGASLMDPN KFLLLVLQRY ELAEA FNKTISTK DQDLI KQYNT OIGASLMDPN FILL I R FILL
EVAYKFPELL EVAYKFPELL GAI SRLHEFV GAVSRLHEFV	YYYHNVKCRR YYYHNVKCRR FYYQDVKCRE FYYQDVKCRE YYVKCR.	YGKRESSEVT YGKRESSEI T FNKTI ST K
AGL HVL L SKS AGL HVL L SKS AGL HVR L SR L AGL HVR L SR L AGL HV L L S	CAQVHAGMMR RNGFSLVNQI YYYHNVKCRR EMFDKDIVMI CAQVHAGMMR RNGFSLVNQI YYYHNVKCRR EMFDKDVVMI VAQVVAEMMR RNGLSLISQV FYYQDVKCRE EMYDKDIIML VAQVVAEMMR RNGLSLISQV FYYQDVKCRE EMYDKDIIMI · AQV. A. MMR RNG. SL. · Q. · YY. · VKCR. EM. DKDIIMI	ELYQLFSTPD ELYQIFSTPD ELTDA ELAEA
RYCVSQEKV SIHLPISRLL AGLHVLLSKS EVAYKFPELL PLSELSPPMLYCVSQEKV SIHLPVSRLL AGLHVLLSKS EVAYKFPELL PLSELSPPMLSYKVSEDLV SIHLPLSRTL AGLHVRLSRL GAISRLHEFV PFDSFQVEVLXSYRVSEDLV SIHLPLSRTL AGLHVRLSRL GAVSRLHEFV SFEDFQVEVLXYVSEDLV SIHLPLSRTL AGLHVRLSRL GAVSRLHEFV SFEDFQVEVLYVVSV SIHLP.SR.L AGLHV.LS	EHPLRCLVL CAQVHAGMMR RNGFSLVNQI EHPLRCLVL CAQVHAGMMR RNGFSLVNQI EYPLRCLVL VAQVVAEMMR RNGLSLISQV EYPLRCLVL VAQVVAEMMR RNGLSLISQV EYPLRCLVL AQVVAEMMR RNG.SLQ.	GVSMMDPN HFLM MLSRF ELYQLFSTPD YGKRFSSEVT HKDVVQQNNTGVSMMDPN HFLM MLSRF ELYQIFSTPD YGKRFSSEIT HKDVVQQNNTGASI MDPN KFLLLVLQRY ELTDA FNKTISTK DQDLIKQYNTGASLMDPN KFLLLVLQRY ELAEA FNKTISTK DQDLIKQYNTG.S. MDPN FILIR FILIR
I RYCVSQEKV I YCVSQEKV KSYKVSEDLV KSYRVSEDLV Y. VS V	I EHPLRCLVL I EHPLRCLVL VEYPLRCLVL VEYPLRCLVL	OT GVS MWDPN OT GVS MWDPN OI GAS I MDPN OI GAS L MDPN O. G. S. MDPN
mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us
6 1 2 2 2	6 1 1 5	6 1 2 2

Figure 1F

798 798 788 788 800	848 848 838 838 850	898 898 888 888
KREII HQLSI KPMAHSELVK KREII HQLSI KPMAHSELVK MREITHLLCI EPMPHSAIAR MREIIHLLCI EPMPHSAIAK REIIH.L.I PM HSK	KEFNLYFYHF KEFNLYFYHF KDFNMYFYHY KDFNMYFYHY K FN. YFYH.	VNI L QCDVML VNI LQSDVML VNL LSCDVM I NL LNCDI MM VN. L. CDVM
	GMYELKPECA GMYELKPECA GVYELKDESL GVYELKDESL G. YELK. E	PPFCPLFASL PPFCPLFASL PFFCPAFSKV PEFCPAFSKV PFFCPAFSKV
MLVGERFNPG VGQVAATDEI MLVGERFSPG VGQVNATDEI YI VGERYVPG VGNVTREEVI YI VGERYVPG VGNVTKEEVT	SLPEDENKET GMESVIESVA HFKKPGLTGR GMYELKPECA KEFNLYFYHF SLPEDENKET GMESVIEAVA HFKKPGLTGR GMYELKPECA KEFNLYFYHF NLPENENNET GLENVINKVA TFKKPGVSGH GVYELKDESL KDFNMYFYHY NLPENENNET GLENVINKVA TFKKPGVSGH GVYELKDESL KDFNMYFYHY NLPENENNET GLENVINKVA TFKKPGVSGH GVYELKDESL KDFNMYFYHY	
MLVGERFSPO MLVGERFSPO YIVGERYVPO YIVGERYVPO	T GMESVIESV/ T GMESVIEAV/ GLENVINKVA T GLENVINKV/	· ·
LI EEMLYLI I LI EEMLYLI I LI EEMLQVLI I	SLPEDENKET SLPEDENKET NLPENENNET NLPENENNET LPE. EN. ET	SRAEQSKAEE SRAEQSKAEE SKTQHSKAEH SKTQHSKAEH SSKAE.
mouse_E3αII human_E3αII mouse_E3αI human_E3αI Consensus	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us	mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3αI Cons ens us
6 1 2	4 4 2 2	6 1 2

Figure 1G

	SEQ I D NO: 6 mouse_E3αII	YI MGTI L QWA	YIMGTILQWA VEHHGSAWSE SMLQRVLHLI	S ML QRVL HL I	GMALOEEKHH	GMAL OE EKHH I FNAVF GHVO	948
human_E3αI]	E3aII	CI MGTI LQWA	VEHNGYAWSE SMLQRVLHLI	S ML QRVL HLI	GMAL QE EKQH LENVTEEHVV	LENVTEEHVV	948
mouse_E3al	_E3αl	YI LRTI FERA	YILRTIFERA VDTESNLWTE GMLQMAFHIL	GML QMAFHI L	ALGLLEEKQQ LQKAPEEEV-	L QK APEEEV-	937
humar	human_E3αl	YI LRTVFERA	YI LRTVFERA I DTDS NLWTE GML QMAFHI L	GML QMAF HIL	ALGLLEEKQQ LQKAPEEEV-	L QK AP E E E V -	937
Conse	Consensus	YI TI A	YITIA VW.E.MLQH	. MLQ H	L. EEKQ. L A. EE. V.	L A. EE. V.	950
snow	mouse_E3aII	TETETOKI SK	TFTFTOKISK PGDAPHNSPS ILAMLETLON APSLEAHKDM	ILAMLETLON	APSLEAHKDM	I RWLLKWFNA	966
humaı	human_ $E3\alpha II$	TETETQKI SK	TFTFTQKISK PGEAPKNSPS ILAMLETLQN APYLEVHKDM	ILAMLETLON	APYLEVHKDM	I RW LKTFNA	966
snau	mouse_E3αl	AF DF Y HKAS R	AFDFYHKASR LGSSAMNAQN I QMLLERLKG I POLEGOKDM I TWILQMFDT	I QMLLERLKG	I PQL EGQKDM	I TW LOWF DT	987
huma	human_E3αl	TFDFYHKASR	TFDFYHKASR LGSSAMNIOM L LEKLKG I PQLEGOKDM I TW LQMFDT	LLEKLKG	I PQLEGQKDM	I TW LOWF DT	984
Conse	Cons ens us	TF. F K. S.	TF. F K. S G N I LE. L P. LE KDM I . W L. MF	ILE.L	. P. LE KDM		1000
snow	mous e_E3αII	I KKI RECS	SSSPVAEAEG	TI MEESSRDK	DKAERKRKAE	I ARLBREKI M 1046	1046
humaı	human_E3al	VKKMRESS	VKKMRESS PTSPVAETEG TIMEESSRDK	TI MEESSRDK	DKAERKRKAE	I ARLRREKI M 1046	1046
sna.	mouse_E3αl	VKRLREKSCL	VKRLREKSCL VVATTSGLEC I KSEEI THDK	I KSEEI THDK	EKAERKRKAE	AARL HRQKI M 1037	1037
huma	human_E3αl	VKRLREKSCL	I VATTSGSES	I KNDEI THDK	EKAERKRKAE	VKRLREKSCL I VATTSGSES I KNDEI THDK EKAERKRKAE AARLHROKI M 1034	1034
Cons ens us	s n s u s	VK RE C.	 	EE DK	. KAERKRKAE	VK. RE. C E EE DK . KAERKRKAE . ARL. R. KI M 1050	1050

Figure 1H

1094 1094 1087 1084 1100	1144 1144 1137 1134 1150	1193 1193 1184 1181
SDAALTALGP SDMTLTALGP SEASRIALGP SDYSRIALGP SDYSRIALGP		VQAKEQRRQQ VQAKEQRRQQ VQLSSQQ VQLSSQQ
I DENKELFQQ TLELDTSASA TLDSSPPV SDAALTALGP 1094 I DENKELFQQ TLELDASTSA VLDHSPVA SDMTLTALGP 1094 I ETHKLMYDN TSEVTGKEDS I MEEESTSAV SEASRI ALGP 1087 I ETHKLMYDN TSEMPGKEDS I MEEESTPAV SDYSRI ALGP 1084 I ETHKLMYDN TSEMPGKEDS I MEEESTPAV SDYSRI ALGP 1100	OTOVPEPRO FVTCI LCOEE OEVTVGSRAM VLAAFVORST VLSKDRTKTI OTOVPEQRO FVTCI LCOEE QEVKVESRAM VLAAFVORST VLSKNRSKFI RGPAVTEKE VLTCI LCOEE QEVKLENNAM VLSACVOKST ALTOHRGKPV (RGPSVTEKE VLTCI LCOEE QEVKI ENNAM VLSACVOKST ALTOHRGKPI	HTGSCGHVMH AHCWQRYFDS VQAKEQRRQQ 1193 HTSSCGHI MH AHCWQRYFDS VQAKEQRRQQ 1193 YTGSCGHVMH AVCWQKYFEA VQLSSQQ 1181 YTGSCGHVMH AVCWQKYFEA VQLSSQQ 1181 TGSCGHVMH A.CWQ YF.
AQMS E MQR HF I DE NKEL F QQ AQMS E MQR HF I DE NKEL F QQ AQMS AL QK NF I ET HKL MY DN AQMS AL QK NF I ET HKL MY DN AQMS . Q. F I K	AQTQVPEPRQ FVTCI LCQEE QEVTVGSRAM VLAAFVQRST VLSKDRTKTI TQTQVPEQRQ FVTCI LCQEE QEVKVESRAM VLAAFVQRST VLSKNRSKFI KRGPAVTEKE VLTCI LCQEE QEVKLENNAM VLSACVQKST ALTQHRGKPV KRGPSVTEKE VLTCI LCQEE QEVKI ENNAM VLSACVQKST ALTQHRGKPI ************************************	AD-PEKYDPL FMHPDLSCGT HTGSCGHVMH AHCWQRYFDS VQAKEQRRQQ 1193 QD-PEKYDPL FMHPDLSCGT HTSSCGHI MH AHCWQRYFDS VQAKEQRRQQ 1193 DHLGETLDPL FMDPDLAHGT YTGSCGHVMH AVCWQKYFEA VQLSSQQ 1181 ELSGEALDPL FMDPDLAYGT YTGSCGHVMH AVCWQKYFEA VQLSSQQ 1181
mo us e_E3aII huma n_E3aII mo us e_E3aI huma n_E3aI Co ns e ns us	mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3α Cons ens us	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us
6 1 2 2	6 1 2 2	6 1 5 2 2

Figure 11

		•
1241 1241 1233 1230 1250	1290 1290. 1283 1279 1300	1340 1340 1333 1329
LRLHTSYDV ENGEFLCPLC ECLSNTVIPL L-LPPRSILS RRLN-FSDQP 1241 LRLHTSYDV ENGEFLCPLC ECLSNTVIPL L-LPPRNIFN NRLN-FSDQP 1241 I HVDL-FDL ESGEYLCPLC KSLCNTVIPI I PLQPQKI NS ENAEALAQLL 1233 I HVDL-FDL ESGEYLCPLC KSLCNTVIPI I PLQPQKI NS ENADALAQLL 1230 I HVDL-FDL ESGEYLCPLC KSLCNTVIPI I PLQPQKI NS ENADALAQLL 1230	SSEDTEAMNI IPIPEGFRPD 1290 STKNSENVDE LQLPEGFRPD 1290 LFNQGMGDST FEFHSILSFG 1283 FFNQGMGDST LEFHSILSFG 1279	YPRNPYSDS I KEMLTTFGT AAYKVGLKVH PNEGDPRVPI LCWGTCAYTI 1340 RPKI PYSES I KEMLTTFGT ATYKVGLKVH PNEEDPRVPI MCWGSCAYTI 1340 25 SVKYSNS I KEMVI LFAT TIYRI GLKVP PDELDPRVPM MTWSTCAFTI 1339 ESSI KYSNS I KEMVI LFAT TIYRI GLKVP PDERDPRVPM LTWSTCAFTI 1329
ENGEFLCPLC ECLSNTVIPL L-LPPRSILS RRLN-FSDQP ENGEFLCPLC ECLSNTVIPL L-LPPRNIFN NRLN-FSDQP ESGEYLCPLC KSLCNTVIPI IPLQPQKINS ENAEALAQLL ESGEYLCPLC KSLCNTVIPI IPLQPQKINS ENADALAQLL E. GE. LCPLC L. NTVIP L. P I. S	QQ! KVVQMLR RKHNAA-DTS SSEDTEAMNI IPIPEGFRPD QQI KALQFLR KEESTP-NNA STKNSENVDE LQLPEGFRPD ARI SGYNI KH AKGEAPAVPV LFNQGMGDST FEFHSILSFG ARI SGYNI RH AKGENP-IPI FFNQGMGDST LEFHSILSFG	FYPRNPYSDS I KEMLTTFGT AAYKVGLKVH PNEGDPRVPI LCWGTCAYTI FRPKI PYSES I KEMLTTFGT ATYKVGLKVH PNEEDPRVPI MCWGSCAYTI VQSSVKYSNS I KEMVI LFAT TI YRI GLKVP PDELDPRVPM MTWSTCAFTI VESSI KYSNS I KEMVI LFAT TI YRI GLKVP PDERDPRVPM LTWSTCAFTI
ENGEFLCPLC ECLSNTVI PL ENGEFLCPLC ECLSNTVI PL ESGEYLCPLC KSLCNTVI PI ESGEYLCPLC KSLCNTVI PI E. GE. LCPLC L. NTVI P.	QQI KVVQMLR RKHNAA- DTS QQI KALQFLR KEESTP- NNA ARI SGYNI KH AKGEAPAVPV ARI SGYNI RH AKGENP- I PI	AAYKVGL KVH ATYKVGL KVH TI YRI GL KVP TI YRI GL KVP
LRLHTSYDV ENGEFLCPLC ECLSNTVIPL LRLHTSYDV ENGEFLCPLC ECLSNTVIPL I HVDL-FDL ESGEYLCPLC KSLCNTVIPI I HVDL-FDL ESGEYLCPLC KSLCNTVIPI I HVDL-FDL ESGEYLCPLC CSLCNTVIPI I HVDL-FDL ESGEYLCPLC KSLCNTVIPI	DLAQWIRAVT QQI KVVQMLR RKHNAA- DTS SSEDTEAMNI NLTQWIRTIS QQI KALQFLR KEESTP- NNA STKNSENVDE TLARW QTVL ARI SGYNI KH AKGEAPAVPV LFNQGMGDST TLARW QTVL ARI SGYNI RH AKGENP-I PI FFNQGMGDST TLARW QTVL ARI SGYNI RH AKGENP-I PI FFNQGMGDST	FYPRNPYSDS I KEMLTTFGT AAYKVGLKVH FRPKI PYSES I KEMLTTFGT ATYKVGLKVH VQSSVKYSNS I KEMVI LFAT TI YRI GLKVP VESSI KYSNS I KEMVI LFAT TI YRI GLKVP
RLRLHTSYDV RLRLHTSYDV RIHVDL-FDL RIHVDL-FDL RD.	DLAQWIRAVT NLTQW RT! S TLARW QTVL TLARW QTVL . LA. W. TV.	FYPRNPYSDS FRPKI PYSES VQSSVKYSNS VESSI KYSNS
mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us	mous e_E3aII huma n_E3aII mous e_E3aI huma n_E3aI Cons ens us	mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3αI Cons ens us
6 4 1 2	6 1 2 2	6 1 1 5 2 2

Figure 1J

1390 1390 1383 1379 1400	1437 1437 1433 1429 1450	1482 1482 1483 1475
SFAAAHWTVA LLPVVOGHFC SFAAAHWTVA SVSVVQGHFC 2FAVAQRATC PQVLIHKHLA QFAVAQRITC PQVLIQKHLV FA.AQ.H	DFSGSSL DFSGISL DTVDLQPSPL DPVDLQPSSV D	TGEEELAILS 1482 PCEEESAVLA 1482 DSEEARCASA 1483 DSEEAHSASS 1475
RFAAAHWTVA RFAAAHWTVA QFAVAQRATC QFAVAQRITC FA . A	VLAFPALQCQ VLAFPALQCQ VLAFPSLYWD VLAFPSLYWD	GMDQENP GMDQENP PGPPLAEGEE PLAQVQE
RLDDCLRSLT RLDDCLRSLT RQHSGLKALM RQHNGLKALM RLL.	IDMFHLLVGL IDMFHLLVGL VDLFHVLVGA IDLFHVLVGA ID. FH. LVG.	ILLTSCTEEN ILLTSCTEEN ILLTTDTDLS ILLTVDTGL-
EKPVFGPLPC DKPLFGPLPC GKPLFGALQN GKPLFGALQN . KPLFG . L	SYEDLPCILD SHEELPCILD QSENTPGLLS KSEDTPCLLS EPC.L.	TGDLHIF HLVTMAHIVQ ILLTSCTEEN TGDLHIF HLVTMAHIIQ ILLTSCTEEN SSYNHLYLF HLITMAHMLQ ILLTTDTDLS SSYNHLYLF HLITMAHMLQ ILLTVDTGL-
QSIERILSDE QSIERILSDE QAIENLLGDE QAIENLLGDE Q IE L .DE	KLFASLVPSD KLFASLVPND RLLSVILPNL RLLSVVLPNI	ATGDLHIF GTGDLHIF SSSYNHLYLF SSSYNHLYLF
SEQ ID NO: 6 mouse_E3αII 4 human_E3αII 15 mouse_E3αI 2 human_E3αI	6 mouse_E3αII 4 human_E3αII 15 mouse_E3αI 2 human_E3αI Consensus	6 mouse_E3αII 4 human_E3αII 15 mouse_E3αI 2 human_E3αI Consensus

Figure 1K

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1581 1581 1583 1575 1600	1631 1631 1633 1625
ESWCQNSEVK ESWCRNSEVK QRWCGDPALL QRWCADPALL	NQASNFSCPK SGGDKSRAPT 1631 NQASNFSCPK SGGDKSRAPT 1631 NQASHFRCPR SADDERKHPV 1633 NQASHFRCPR SADDERKHPV 1625 NQAS F.CP. S.DP. 1650
ENSDIMNSLI ENSEIMNSLI EYWDTIRPLL EYWDTVRPLL	NQASNFSCPK NQASNFSCPK NQASHFRCPR NQASHFRCPR NQAS.F.CP.
LPTNLIHLFQ LPNNLICLFQ LPTNLFLLFQ LPTNLFLLFQ LPTNLFLLFQ	DLPEDYSSLI NLPEDYSSLI ELPEDYSCLL ELPDDYSCLL . LPEDYS . L.
HFEHLCNYLS HFEHLCSYLS EFSALCSYLS EYSALCSYLS . F LCSYLS	SYPRGANKLI RYPRESNKLI RYPRKRNSLI RYPRKRNSLI
PDLQV-SGTS PDIQV-PGTS EELFANSAEG EELHTNSAEG	RYLNGERGAI RYLEGERDAI KSLKQKSAVV NCLKOKNTVV
6 mouse_E3aII 4 human_E3aII 15 mouse_E3aI 2 human_E3 aI	6 mouse_E3αII 4 human_E3αII 15 mouse_E3αI 2 human_E3αI Consensus
	PDLQV-SGTS HFEHLCNYLS LPTNLIHLFQ PDIQV-PGTS HFEHLCSYLS LPNNLICLFQ EELFANSAEG EFSALCSYLS LPTNLFLLFQ EELHTNSAEG EYSALCSYLS LPTNLFLLFQLS FLCSYLS LPTNLLFQ

Figure 1L

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1681	1683	1700	1731	1731	1733	1725	1750					•
I FLRVRECQV I FLRVRECQV	I FLKI RECRV I FLKI RECRV	I FL REC. V	RKI QKL WQQH	KKI OKL WHQH	RKL HL VWQQH	RKL HL VWQQH	RKWQQH					
LCLVCGSLLC SQSYCCQAEL EGEDVGACTA HTYSCGSGAG IFLRVRECQV 1681 LCLVCGSLLC SQSYCCQTEL EGEDVGACTA HTYSCGSGVG IFLRVRECQV 1681	LCLECGALLC SONI CCOELV NGEEVGACVE HALHCGAGVC LELKI RECRV 1683 LCLECGALLC SONI CCOELV NGEEVGACLE HALHCGAGVC LELKI RECRV 1675	LCL. CG LC SQ CCQ GE. VGAC H CG. GV. IFL REC. V 1700	LFLAGKTKGC FYSPPYLDDY GETDQGLRRG NPLHLCQERF RKI QKLWQQH 1731	RG NPLHLCKERF	VLVEGKARGC AYPAPYLDEY GETDPGLKRG NPLHLSRERY RKLHLVWQQH 1733	VLVEGKARGC AYPAPYLDEY GETDPGLKRG NPLHLSRERY RKLHLVWQQH	GK GC . Y PYLD. Y GETD. GL. RG NPLHL ER. RK WQQH	1755	1755	1757	1749	1774
EGE DVGAC EGE DVGAC	NGE EVGAC\	. GE. VGAC	GET DQGL R	GET DQGL R	GET DP GL KF	GETDPGLK	GETD. GL.	WOHL	WQHL	MQLL	WQLL	WQ. L
S QS Y C C Q A E L S QS Y C C Q T E L	SQNI CCQEI V SQNI CCQEI V	SQ CCQ	FYSPPYLDDY	FYSPPYLDDY	AYPAPYLDEY	AYPAPYLDEY	. Y PYLD. Y	E ANQT LVGI D	E ANQT L VGI D	ET NOML FGF N	HEELARSQ ETNOMLEGEN WOLL	I. EEI Q E. NQ. L. G WQ. L
TCLVCGSLLC LCLVCGSLLC	LCLFCGAILC LCLFCGAILC	LCL. CG LC	LFLAGKTKGC	LFLAGKTKGC	VLVEGKARGC	VL VEGKARGC	GK GC	SI TEEI GHAQ EANQTLVGI D WQHL	SVTEEI GHAQ EANQTLVGI D WQHL	CITEEL ARSQ ETNOMLFGFN WOLL	CI I EEI ARSQ	. I . EEI 0
\vdash		Consensus	mouse_E3aII	human_ $E3\alpha II$	mouse_E3al	human_E3αl	Consensus	mous e_E3aII	human_E3αII	mouse_E3αl	human_E3al	Cons ens us
0 4 -	2 .		9	4	15	7		9	4	15	7	